

- (d) preparing an implant adapted for placement at said site and including said genetically produced growth factor;
  - (e) placing said implant at said selected implant site.--

## **REQUEST FOR RECONSIDERATION**

The Examiner's thoughtful attention to this application is sincerely appreciated.

Reconsideration of the rejections stated in the Office Action of May 27, 1999 is respectfully requested in view of the foregoing amendments and the following remarks.

## The Invention

According to the invention, Applicant provides an improved process for inducing the growth of a blood vessel. Applicant's Specification states that:

A. Genetically produced materials are used to grow any desired soft and hard tissue.

*“As would be appreciated by those skilled in the art, genetically produced material can be inserted in the body to cause the body to grow, reproduce, and replace leg bone, facial bone, and any other desired soft and hard tissue in the body.”* Specification, p. 31, lines 24 to 26. [U.S. Patent No. 5,397,235: Col 21, lines 22 to 26]

1      B.    **Growth factors can be utilized to grow soft or hard tissue.**

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3      "Growth factors can be utilized to induce the growth of "hard tissue" or bone  
4      and "soft tissues" like ectodermal and mesodermal tissues. As used herein, the  
5      term growth factor encompasses compositions and living organisms which  
6      promote the growth of hard tissue, such as bone, or soft tissue in the body of a  
7      patient. The compositions includes organic and inorganic matter." Specification,  
8      p. 20, lines 10 to 14 [U.S. Patent No. 5,397,235, Col. 14, lines 4 to 10]

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10     C.    **Growth factors can be genetically produced or manipulated.**

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12     "The compositions can be genetically produced or manipulated. The living organisms  
13     can be bacteria, viruses, or any other living organism which promote tissue growth."  
14     Specification, p. 20, lines 14 to 16 [U.S. Patent No. 5,397,235; Col. 14, lines 10 to 14]

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16     D.    **Many different growth factors can be utilized to grow hard or soft tissue.**

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18     "By way of example and not limitation, growth factors can include platelet-derived  
19     growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor  
20     (acidic/basic)(FBG a,b), interleukins (IL's), tumor necrosis factor (TNF),  
21     transforming growth factor (TGF-B), colony-stimulating factor (CSF), osteopontin  
22     (Eta-1)(OPN), platelet-derived growth factor (PDGF), interferon (INF), bone  
23     morphogenic protein 1 (BMP-1), and insulin growth factor (IGF)." Specification, p.  
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1           20, lines 16 to 21 [U.S. Patent No. 5,397,235: Col 14, lines 14 to 23]

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3       **E. The growth factors can include genetic material.**

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5           *"Recombinant and non-recombinant growth factors can be utilized as desired."*

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7           Specification, p. 20, lines 21 and 22 [U.S. Patent No. 5,397,235: Col. 14, lines 23 and 24]

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9           *"The growth factors can be multifactorial and nonspecific."* Specification, p. 21, lines 14

10          and 15 [U.S. Patent No. 5,397,235: Col. 14, lines 60 and 61].

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12       **F. Growth factors can be applied in gels or other carriers.**

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15           *"Growth factors can be applied in gels or other carriers which regulate the rate of*

16          *release of the growth factors and help maintain the growth factors, and the carrier, at a*

17          *desired location in the body."* Specification, p. 20, lines 26 to 28 [U.S. Patent No.

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19          5,397,235: Col. 14, lines 31 to 35].

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21           *"The growth factor can be administered orally, systemically, in a carrier, by hypodermic*

22          *needle, through the respiratory tract, or by any other desired method."* Specification, p.

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24          21, lines 4 to 6 [U.S. Patent No. 5,397,235: Col. 14, lines 43 to 46]

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26       **G. The growth factor can control cell growth, function, and migration.**

1       “*Either the carrier or the growth factor can mimic extracellular fluid to control cell*  
2       *growth, migration, and function.*” Specification, p. 21, lines 3 and 4 [U.S. Patent No.  
3                   5,397,235: Col. 14, lines 41 to 43]  
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6       H. ***Genetically produced material can be utilized to grow an organ.***

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8       “In another embodiment of the invention, genetically produced living material is  
9       used to form an implant in the bone of a patient. The DNA structure of a patient  
10      is analyzed from a sample of blood or other material extracted from a patient and  
11      a biocompatible tooth bud 122 is produced. The bud 122 is placed in an opening  
12      123 in the alveolar bone and packing material is placed around or on top of the  
13      bud 122.” Specification, p. 30, lines 14 to 18. [U.S. 5,397,235: Col. 21, lines 1 to  
14                   8]  
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18       “In another embodiment of the invention, instead of transplanting a bud 122 into  
19       the jaw of a patient, a quantity of genetically produced living material which  
20       causes bud 122 to form in the alveolar bone can be placed at a desired position in  
21       the alveolar bone such that bud 122 is morphogenetically created in vivo and  
22       grows into a full sized tooth. Instead of forming an opening 123, a needle or other  
23       means can be used to simply inject the genetically produced living material into a  
24       selected location in the alveolar bone.” Specification, p. 31, lines 18 to [U.S.  
25                   Patent No. 5,397,235: Col. 21, lines 14 to 22]  
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1       The Use of Genetically Produced Material to Grow Organs Was Known in 1993.

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3       The article "How Limbs Develop" (*Scientific American*, February 1999, pp. 74 to  
4       79)(copy attached) describes how in the *summer of 1993* an *implant* of *Sonic hedgehog gene* or  
5       *fibroblast growth factor* was used to produce a growth factor which caused bone, muscle, blood  
6       vessels and skin to grow:

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9       " ... we spliced the Sonic hedgehog gene into embryonic chick cells grown in the  
10      laboratory, causing the cells to produce the Sonic hedgehog protein, and then  
11      implanted the cells into the anterior side of a chick limb bud." Page 78, 1<sup>st</sup>  
12      Column, bottom paragraph; illustrations, p. 76.

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15      As can be seen from the Scientific American article, in 1993 the technology for implanting  
16      genetically produced material was available and was not complicated.

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19      Growth of Blood Vessels with Genetically Produced Material has been Accomplished

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21      The *Isner reference* (copy attached without drawings) (U.S. 5,652,225) specifically  
22      Claims a method for **inducing the formation of new blood vessels** in a human host.

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25      The *Isner reference* appears to utilize the process set forth in Applicant's Specification.

26      In particular:

1. Isner utilizes genetically produced material, namely VEGF or another growth factor produced by a DNA segment, to induce growth of a blood vessel. For example, Claim 1 of *Isner* specifically sets forth "...a first DNA encoding an angiogenic protein ..." (Page 2 of Isner, at bottom).
  2. *Isner* also sets forth in Claim 1 a list of growth factors nearly **identical** to the list of growth factors set forth at Col. 14 of Applicant's Specification. The growth factors sets forth by *Isner* in his Claim 1 are:

"...acidic and basic fibroblast growth factors, vascular endothelial growth factor, epidermal growth factor, transforming growth factor .alpha. and .beta., platelet-derived endothelial growth factor, platelet-derived growth factor, tumor necrosis factor .alpha., hepatocyte growth factor and insulin like growth factor ..."
  3. *Isner* notes that the above-noted DNA encoding growth factors were set forth in 1987 by Folkman, et al., in *Science* magazine. See the paragraph spanning pp. 7 and 8 of the *Isner* reference.

## **DISCUSSION**

26 The growth of blood vessels with *genetically produced materials* has been demonstrated.  
27 U.S. Patent No. 5,652,225 to *Isner* was issued on one process for accomplishing such. Applicant

1 can, if appropriate, provide other publications demonstrating the growth of blood vessels with  
2 genetically produced materials.  
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4  
5 Applicant's Specification sets forth the use of ***genetically produced materials***, including  
6 growth factors, to grow organs and hard and soft tissue.  
7

8 The **genetically produced growth factors** set forth in the *Isner reference* to induce the  
9 growth of blood vessels **are specifically set forth in Applicant's Specification**, as is the fact  
10 that growth factors can be used to induce the growth of organs and other hard and soft tissue.  
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12 **The Isner patent resulted from an application filed on October 4, 1994, about one year after**  
13 **Applicant's parent application was filed on July 2, 1993.**

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15 As evidenced by the *Isner reference* and the Scientific American article, **implanting a**  
16 **gene or growth factor is not a complicated process, and the procedures for accomplishing such**  
17 **are known in the art.**

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20 Consequently, Applicant respectfully submits that the foregoing, taken in conjunction  
21 with the amended Claims, remedies the Section 101 and 112 rejections.  
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24 **The New Claims**

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26 The foregoing amendment cancels original Claims 1 and 3 to 5, amends Claim 2, and  
27 inserts new Claim 6.  
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## CONCLUSION

By recognizing the functional advantages of providing an improved process for inducing the growth of blood vessels, and by providing novel process steps to accomplish such, Applicant provided a process not previously recognized by those of ordinary skill in the art.

If the Examiner finds merit in the foregoing remarks and amendments, it is believed the application is in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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